(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
18 September 2003 (18.09.2003)

PCT

(10) International Publication Number
WO 03/075771 A1

(51) International Patent Classification[7]: A61B 8/08, 8/14, G01S 15/89

(21) International Application Number: PCT/US03/04413

(22) International Filing Date: 14 February 2003 (14.02.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
10/094,844 8 March 2002 (08.03.2002) US

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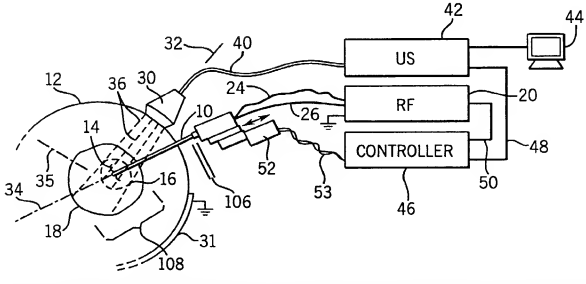
(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: ELASTOGRAPHIC IMAGING OF SOFT TISSUE IN VIVO



(57) Abstract: Elastographic images provide visualization in two or three dimensions of RF ablation lesions to guide in the ablation process. Compression may be applied using the RF probe. A similar technique may be applied to *in vivo* imaging of soft tissue without ablation.

WO 03/075771 A1

ELASTOGRAPHIC IMAGING OF SOFT TISSUE IN VIVO

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] --

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

[0002] --

BACKGROUND OF THE INVENTION

[0003] The present invention relates to medical imaging, and in particular to methods of *in vivo* elastographic imaging.

[0004] Elastography is a new imaging modality that reveals the stiffness properties of tissues, for example, axial strain, lateral strain, Poisson's Ratio, Young's Modulus or other common stiffness measurements. The measurements provide a two-dimensional array of data in which array location corresponding to tissue locations in an image plane. The array of data may be mapped to a gray scale to form a picture.

[0005] In "quasi-static" elastography, two images of the tissue are obtained. The first image forms a base line of the tissue in an unstressed or relaxed state or under a small pre-compression. The second image is obtained with the tissue under compression. Displacement of the tissue between the two images is used to deduce the stiffness of the tissue. The quasi-static elastogram is analogous to a physician's palpation of tissue in which the physician determines stiffness by pressing the tissue and detecting the amount that the tissue yields under pressure.

[0006] In "dynamic" elastography, a low frequency vibration is applied to the tissue and the velocity of the resulting elastic waves is measured, for example, using ultrasonic Doppler detection. Elastography of both types may be conducted using imaging techniques other than ultrasound, including computed tomography (CT) and magnetic resonance imaging (MRI).

[0007] While elastography has great promise, *in vivo* elastography of soft tissue structures such as the liver and other abdominal organs can be difficult because

externally applied axial compression may induce nonaxial or lateral slippage of the organ. This lateral motion can obscure true axial tissue compression used to deduce stiffness of the tissue.

SUMMARY OF THE INVENTION

[0008] The present inventors have recognized that compression of the tissue may be done by a probe inserted percutaneously into the tissue to be measured. The probe applies compression in a localized and controlled fashion and may stabilize the tissue against lateral slippage.

[0009] In one embodiment, the probe may be a radio frequency (RF) ablation electrode used for the ablation of soft tissue. The ablation lesion creates a zone of necrosis with greater stiffness than the surrounding tissue.

[0010] While the invention is applicable to a wide variety of imaging modalities, it is well suited for ultrasound imaging commonly used for probe guidance, for example, during RF ablation. Ultrasound imaging is sensitive to the temperature of the tissue as may change the speed of sound used for the imaging. Accordingly, the inventors have also developed a method of compensating ultrasound images for heating during the ablation process and/or of providing a separate thermographic image of the tissue during RF or other methods of ablation.

[0011] The invention makes possible three-dimensional elastography of *in vivo* tissues by collecting elastographic images of adjacent image planes. In the case of RF ablation, this three-dimensional data allows for computation of lesion volume size and position within the treated region .

[0012] Specifically then, one embodiment of the present invention provides a method of monitoring RF ablation of tissue and includes the steps of inserting an ablation electrode into an ablation region of the tissue and applying RF ablation current to the ablation region. The tissue may be subject to dynamic or quasi-static compression to obtain an elastogram demarcating the lesion formed by the RF ablation.

[0013] It is thus one object of the invention to provide a simple and effective method of monitoring lesion size during or after an RF ablation.

[0014] The compression of the tissue may be performed by the RF ablation probe.

[0015] It is an object of this embodiment of the invention to apply precise compression to the region of interest, *in vivo,* with minimal lateral slippage. The probe provides a concentrated compressive force undiffused by intervening tissue and serves to stabilize the region while it is compressed.

[0016] The invention may include monitoring periodic physiological motion and acquiring a compression and baseline image, compared to produce the elastogram, in a period of minimal periodic physiological motion such as breathing or the like.

[0017] Thus, it is the object of one embodiment of the invention to minimize other sources of tissue movement when external or probe compression is applied.

[0018] Alternatively, the monitoring of the period physiological motion may be used to time the acquisition of the compression image at maximum compression caused by the periodic physiological motion and the baseline image at a period of minimal compression caused by the period physiological motion.

[0019] An object of this embodiment of the invention is to image an RF ablation lesion using naturally occurring compression of the tissue.

[0020] The invention may include the step of obtaining measurements of temperature increases caused by the RF ablation.

[0021] It is an object of this embodiment of the invention, therefore, to provide the ability to correct the elastogram of the lesion for temperature effects and/or to produce a thermographic image of the lesion and the surrounding tissue.

[0022] The method may include the steps of obtaining multiple images of planes through the tissue to produce a three-dimensional image indicating elasticity of the tissue in the region.

[0023] Thus, it can be an object of some embodiments of the invention to provide an image that may be used for better visualization of a lesion and/or for the calculation of its volume and the like.

[0024] More generally, the invention relates to the use of a probe to apply compression to tissues for elastographic imaging even when ablation is not contemplated.

[0025] It thus can be an object of the invention to provide for elastographic imaging of structures such as organs that are otherwise not easily compressed using external compression.

[0026] The images may be obtained using ultrasonic imaging techniques applying ultrasonic energy propagating along an insonification axis, and the probe may compress the tissue along the insonification axis. Further, the probe may be inserted along the insonification axis.

[0027] Thus, it is another object of the invention to provide for controlled lateral motion of the imaged organ when directional imaging techniques such as ultrasound are used.

[0028] The present invention makes practical three-dimensional elastographic imaging of *in vivo* tissue in which multiple elastographic images are obtained for multiple adjacent planes. The results of these images may be assembled to display a three-dimensional representation of, for example, an RF ablation lesion, or used for other three-dimensional operations including volume or perimeter calculations.

[0029] Thus, it is another object of the invention to provide for three-dimensional imaging of soft tissue within a patient using elastography.

[0030] The foregoing objects and advantages may not apply to all embodiments of the inventions and are not intended to define the scope of the invention, for which purpose claims are provided. In the following description, reference is made to the accompanying drawings, which form a part hereof, and in which there is shown by way of illustration, a preferred embodiment of the invention. Such embodiment also does not define the scope of the invention and reference must be made therefore to the claims for this purpose.

BRIEF DESCRIPTION OF THE FIGURES

[0031] Fig. 1 is a simplified block diagram of an RF ablation system for use with the present invention showing insertion of an ablation probe into a tumor site of an *in vivo* organ, an ultrasonic imaging system for imaging of the organ and tumor site, and further showing a control system for applying controlled quasi static compression to the tumor site through the RF ablation probe;

[0032] Fig. 2 is a graphical representation of an ultrasonic waveform received by the ultrasonic imaging system of Fig. 1 such as forms a single line of a B-scan ultrasonic image, the waveform shown before and after compression and showing a shifting of the signal corresponding to tissue movement within the tissue under compression;

[0033] Fig. 3 is a block diagram of the processing of the scan data of Fig. 2 to deduce tissue stiffness using a time-domain analysis technique;

[0034] Fig. 4 is a figure similar to that of Fig. 3 using a frequency-domain analysis technique;

[0035] Fig. 5 is a perspective representation of an ablation lesion reconstructed from multiple elastographic images taken in several adjacent planes according to techniques of Figs. 1-4 above;

[0036] Fig. 6 is a graph showing compression, respiration, acquisition of images, and temperature, each as a function of time and illustrating different ablation schedules according to the present invention;

[0037] Fig. 7 is a simplified elastographic image of a lesion according to the techniques of Figs. 1-6;

[0038] Fig. 8 is a simplified thermographic image obtained as part of the ultrasonic elastogram;

[0039] Fig. 9 is a simplified representation of the process of deducing tissue movement per Fig. 3 showing the problem of decorrelation with rapid temperature rise;

[0040] Fig. 10 is a flowchart showing the steps of producing the images of Fig. 7 and 8; and

[0041] Fig. 11 is a detailed flowchart showing the calculation of temperature over periods of possible decorrelation per Fig. 9.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

[0042] Referring now to Fig. 1, an RF ablation probe 10 may be inserted percutaneously into a patient 12 to have its tip located at an ablation region 16 within an organ 18 such as the liver.

[0043] Extensible electrode tines 14, at the tip of the probe 10, may grip the tissue of the ablation region and provide a greater area of electrical contact to conduct

ablative current from an RF source 20. Electrical energy from the RF source 20 is conducted through an insulated shaft of the probe 10 to the conductive tines 14 where ionic heating of the tissue kills tumor tissue. A large-area grounding pad 31 placed on the patient's skin provides a return path for this current. The tines 14 may include thermocouples for temperature measurements.

[0044] RF ablation probes 10 of this kind having extensible tines and thermocouple sensors are well known in the art and readily available. The RF 20 source may be a Rita Model 30 electrosurgical device manufactured by Rita Medical Systems Inc., Mountain View, California or other similar deviee.

[0045] During the ablation process, electrical current is conducted from the RF source 20 along line 26 to the ablation probe 10. The temperature signal is returned along line 24 to be received by the RF source 20 and used to limit the temperature of ablation according to techniques well understood in the art.

[0046] Location of the probe 10 may be done using any ultrasonic imaging system, for example, the Acuson 128 XP Real Time Scanner manufactured by Acuson Incorporated of California. The ultrasonic imaging system includes an ultrasonic transducer 30 and ultrasonic processing electronics 42. The ultrasonic transducer 30 may be, for example, a linear array transducer approximately forty millimeters wide, operating with dynamic focus over a forty percent bandwidth and producing signals at a center frequency of five megahertz. Generally, 1D, 1.5D and 2D transducers 30 are suitable for the image generating process.

[0047] During insertion of the probe 10, the ultrasound transducer 30 is placed against the skin of the patient and moved as needed for accurate visualization of the tip of the probe 10 with respect to the organ 18.

[0048] During the elastographic imaging to be described, the axis 32 of the ultrasound transducer 30 (along which the signals 36 propagate) is aligned as close as possible to the axis 34 along which the probe 10 is inserted and directed to send the ultrasonic signals 36 into the ablation region 16. The probe 10 stabilizes the organ 18 and prevents lateral shifting along axis 35.

[0049] During both procedures, each signal 36 travels into the tissue and is reflected at various tissue structures and boundaries. These echoes are detected by the

ultrasound transducer 30 and conducted by cable 40 to the ultrasound processing circuitry 42. The received signals are digitized at a sampling rate of approximately 50 megahertz and then processed according to techniques well known in the art, to produce an image, for example, a B scan image, on display terminal 44. The signals 66 lie generally along a plane incorporating axis 34 and defining an image plane of the B-scan image.

[0050] According to the invention, the digitized echo signals may be further processed within the ultrasonic processing circuitry 42 to produce an elastographic image or may be transmitted to a separate controller 46 for processing there, as will be described. In the former case, line 48 communicates signals from the controller 48 to the ultrasonic processing circuitry 42 to coordinate generation of the elastographic image, in the latter case line 48 carries the control signals from the ultrasound system and digitized echo signals from the ultrasonic processing circuitry 42 to the controller 48 for processing by the controller 48.

[0051] The controller 46, which may be a computer or logic controller programmed, as described below, also receives temperature information via the RF source 20 along cable 50. This temperature information may also be used to provide control signals to the RF source 20 from the controller 48 to further control the RF ablation as well as to generate and normalize thermographic images as will be described. Controller 46 also provides output lines 53 connected to a motorized carriage 52, for example, one using a stepper motor and a lead screw to provide motion of the probe 10 along its insertion axis 34 in a controlled manner according to signals on output line 53 as will also be described. Other mechanisms for implementing the motorized carriage 52 may be used including those which apply a predetermined compressive force or low frequency oscillation. The controller 46 may also communicate with display terminal 44 for displaying images and receiving user input commands

[0052] Referring now to Fig. 2, signals 36 may be preprocessed by the ultrasound processing circuitry 42 for focusing, noise rejection and the like to produce image signals 56. The varying amplitude of each image signal 56 is mapped to brightness of corresponding pixels 54 forming the columns of the B-scan image 53. Thus, each column of the image 53 is generated from what is essentially a time-domain signal

56 where the time axis also generally reflects distance from the ultrasound transducer 30 to the tissue feature shown in the image 53.

[0053] In quasi-static elastography, the stiffness of the tissue that is the subject of the image 53 may be determined by comparing two ultrasound echo-signal images 53 (made up of signals 56a and 56b, respectively) during different degrees of compression of the tissue. For example, as directed by signals from the controller 46, a first (baseline) signal 56a may be acquired of the ablation region 16 with the tissue uncompressed, or with a first degree of compression. Upon completion of this image acquisition, controller 46 causes an incremental inward movement of the probe 10 causing compression of the tissue of the ablation region 16 by the extended tines 14. A second (compression) signal 56b may then be acquired. This second signal 56b will generally exhibit an expansion in time reflecting a compression of the subject tissues away from the ultrasound transducer 30.

[0054] A general translation of tissue of the ablation region 16 would cause an equal offset between all the points of signals 56a and 56b over time (and hence over distance). However, the elasticity of the tissue causes tissue compression which in turn produces a gradient in the offset of the signals 56a and 56b as a function of time and distance. Generally, the difference 58 between signals 56a and 56b at early times and hence from tissue near the ultrasonic transducer 30 will be smaller than the separation 60 at later times and for tissue further away from the ultrasound transducer 30. The gradient of these displacements over the region of the ablation region 16 produces an elastogram of the tissue of the ablation region 16.

[0055] Referring to Fig. 3, ultrasonic scan data 64 from the ultrasound processing circuitry 42 (being complete image sets of signals 56a and 56b) are processed to determine tissue displacement along an axis from the ultrasound transducer 30 through the ablation region 16 by process block 65. This displacement may be determined by analyzing short segments of signals 56a and 56b and moving one segment with respect to the other until the best match is obtained. The amount of movement needed for the best match determines tissue displacement. The matching process may be implemented by means of mathematical correlation of the segments.

[0056] The displacement of the tissue, represented by displacement signal 66, is further processed by process block 68 which determines strain as the gradient of the displaeement signal 66. The strain signal may be mapped to brightness values in elastographic images 72. Each of the process blocks may be implemented through a combination of hardware and software in controller 46 or ultrasound processing circuitry 42 according to well-known signal processing techniques.

[0057] Referring now to Fig. 7, the elastographic image 72 will provide for a high contrast region 84 showing a zone of tissue necrosis about the tines 14 such as causes a greater stiffness in that tissue. In this way, progress of the ablation may be tracked. Generally, a light band 86 may surround the necrotic tissue representing heated soft tissue, as will be described below, further improving the contrast of the image.

[0058] Referring now to Fig. 5, this process of generating an elastographic image 72 may be repeated with the ultrasound transducer 30 moved to different image planes 70 being parallel and adjacent to each other, or in a fan-like array of planes produced with a tipping of the ultrasonic transducer 30, or other pattern so as to cover an entire volume of the ablation region 16. These multiple planes 70 provide corresponding multiple elastographic images 72. The high contrast regions 84 of each of the elastographic images 72 may be assembled to define a three-dimensional volume of the actual lesion. Such a three-dimensional data set allows computation of lesion volume and lesion shape and may better indicate the location and orientation of the lesion.

[0059] Referring now to Fig. 4, alternative algorithms may be used to create the elastographic images 72. In one such algorithm, the signals 56a and 56b may be received by process block 80 to extract a spectra of the signals 56a and 56b using, for example, the well-known fast Fourier transform algorithm. The spectra of the signals 56a and 56b will be shifted according to the Fourier transformation property that causes dilation in a time-domain signal to produce a down-frequency shift in its frequency-domain spectrum. The amount of shift may be determined at process block 82 using correlation techniques similar to those used in process block 65 but executed on the frequency-domain signals.

[0060] The shift between the spectra taken of different segments of the time-domain signals 56a and 56b centered at increasing time delays, provides a gradient signal to produce elastographic images 72. While the results are similar to the technique of Fig. 3, this approach may have some advantages in terms of robustness against noise and the like.

[0061] Heating of the tissue of the ablation region 16 during ablation changes the sound speed in the tissue and causes thermal expansion. Both of these effects produce a shift in the signals 56a and 56b similar to that caused by tissue displacement. Accordingly, the present invention, particularly when used with ultrasonic imaging, may be used to deduce the temperature of the ablation region 16 and if desired, to correct the stiffness image for temperature effects and/or produce a thermograph of the tissue. Breathing and other physiological activity may cause additional compression of the tissue. These effects may be moderated by timing of the image acquisitions or may be used to augment or in lieu of the compression provided by the probe 10. A detailed description of such corrections and a more complex protocol for generating elastograms 72 will now be described.

[0062] Referring now to Figs. 1 and 10, at a first step in the ablation protocol, indicated by process block 90, the probe 10 is inserted into the patient 12, as before, using ultrasound or other imaging techniques to locate the tines 14 in the ablation region 16. At process block 92, the tines 14 may be deployed to provide a gripping of the tissue aiding in the compression to follow.

[0063] At this time, the RF ablation may be performed and completed and a baseline and compression image (containing signals 56a and 56b, respectively) acquired and an elastogram calculated of the lesion so formed, with the option of additional RF ablation being continued (with the probe 10 remaining in place) and additional images 53 being taken. Alternatively, the RF ablation may be performed during the time that the images 53 are being obtained, as indicated by bracket 94, for real time representation of the ablation lesion's growth.

[0064] Referring now to Fig. 6, during the period of image acquisition, physiological motion such as respiration of the patient, may be monitored, to time the acquisition of images 56 during periods when no additional compression is being

applied to the tissue such as may alter the derived elasticity. In this regard, a respiration signal 96 may be obtained using a standard chest cuff or the like as is known in the field of magnetic resonance imaging. The respiration signal 96 will exhibit periods 98 of high diaphragm movement and periods 100 of relative quiescence.

[0065] During a first quiescence period 100a, a series of acquisitions 102 of baseline images may be obtained as ablative current is conducted into the tissue and without compression (or with a baseline compression). These baseline acquisitions 102, indicated by process block 115 of Fig. 10) provide a measurement of changes in signals 56a (shown in Fig. 2) resulting not from compression, but from temperature effects. A temperature difference may be calculated by determining the apparent tissue displacement and applying a gradient of tissue displacement to a empirically defined function relating displacement gradient to temperature rise as indicated by subsequent process block 116. Generally, some of the acquisitions used for process blocks 103 and 111 may be shared with process block 115.

[0066] Thus, each acquisition 102 can be used to derive a step in temperature function 104 of corresponding tissue during the period 100a. When the period 98a (of high physiological motion) occurs or no later than the beginning of period 100a of low physiological motion, the probe 10 may be moved to compress the tissue as indicated by signal 109, using the motorized carriage 52. Referring momentarily to Fig. 2, the amount of movement 106 of the probe 10 may be limited to provide approximately 1% compression to the tissue with respect to the total organ size 108. In the preferred embodiment, incremental motion of one millimeter may be used.

[0067] During the next quiescent period 100b, acquisitions 110 may occur providing compression images 53 as indicated by process block 111 of Fig. 10. These compression acquisitions 110 may be compared to themselves to deduce changes in the temperature function 104 (per later process block 116) and compared to the baseline images 53 of acquisition 102 to deduce elasticity per later process block 112.

[0068] Referring still to Fig. 6, at period 100c, a new baseline acquisition 102' may be obtained and this process repeated with additional interleaved baseline and

compressive acquisitions occurring. These later compressive acquisitions may use increased compression, for example, by moving the probe 10 an additional increment up to a compression limit at which time the probe 10 may be retracted to its initial position.

[0069] Referring now to Fig. 9, during the period 98a, when no acquisitions occur, there may be substantial displacement of the signals 56a and 56b caused by temperature effects. It will be understood that beyond a certain displacement of signals 56a and 56b correlation will be lost because there may be multiple local maxima in the correlation, each of which represents a plausible amount of heating or tissue deformation. Accordingly, the amount of temperature change during period 98a is generally not known. To remedy this, at process block 116, an extrapolation of the rate of temperature increase in period 98a may be used as a starting point for measured temperature increases in period 100b. Alternatively, the change in the temperature signal 104 from the thermocouple in the probe 10 may be used to estimate the change in temperature during period 98a.

[0070] Referring now to Fig. 11, within process block 116, at a decision block 128, it is determined whether correlation is likely lost because of a lapse in time. If not, a new change in temperature is calculated for each pixel, at process block 130, based on the apparent tissue displacement of the corresponding portions of signals 56a or 56b. This change in temperature is added to the last known temperature for those pixels at process block 135.

[0071] If correlation is likely lost as determined by process block 128, then as indicated by process block 132, an extrapolated temperature is determined by looking at the rate of historical temperature increase (during period 100a) and or the rate of temperature increase for one pixel indicated by the thermocouple through probe temperature signal 118. This change in temperature is added to the last known temperature for those pixels at process block 135.

[0072] While only a single temperature signal 104 is shown, it will be understood that the invention in fact provides a temperature value for the tissue corresponding to each pixel of the images 53 in the same way that elasticity data is provided for each such pixel.

[0073] Referring again to Fig. 10, at process block 120, a thermal image 122 (shown in Fig. 8) may be generated from this temperature data such as will generally show an increasing region 124 of elevated temperature expanding about the ablation region 16. As indicated by Fig. 10, the temperature information may be used to modify the elasticity information received at process block 112 by subtracting an inferred temperature effect (i.e., the expected shift in the signals 56a and 56b expected from the measured temperature increase and the resultant thermal expansion). For this purpose, the relationship of temperature to offset of signals 56a and 56b need not be known precisely because conversion to absolute temperature need not be performed.

[0074] At process block 126, corrected elastographic images 72 are produced. The process of process block 126 may be repeated to obtain three-dimensional data and outputs of volume, diameter and the like may be provided.

[0075] Referring again to Fig. 6, in an alternative embodiment, the acquisition 110' of compression images may be performed during period 98b of maximum physiological motion eliminating the need for compression by the RF probe and useful in situations where imaging is to be obtained without ablation. This motion of the diaphragm can be used to generate stiffness or strain images. This is done by obtaining a baseline ultrasound echo-signal frame, followed by the post-compression ultrasound echo-signal frame after a specified time-interval.

[0076] Temperature imaging in the absence of physiological motion or other motion artifacts is performed by obtaining a baseline ultrasound echo-signal image and subsequent ultrasound echo-signal images obtained at periodic intervals. Temperature maps display the initial temperature rise and are continuously updated over time. The periodic acquisition of data has to be at a sufficient frame rate to avoid loss of correlation between consecutive frames. We have used a frame rate of 2 frames/sec using the 5 MHz transducer. However, higher frames rates are required for higher frequency transducers and faster rates of temperature increases.

[0077] It will be understood that the techniques described herein are examples that fall within the claims and that a number of variations are possible. For example, although ultrasound imaging is useful for probe location and commonly used, the

techniques described herein may be applied to CT, MRI and other image techniques that provide indication of tissue movement. The technique of compressing tissues with a probe need not include RF ablation and the probe 10 need not be the compressive force when imaging a lesion formed by RF ablation. When a probe is used for compression, it need not be an RF ablation probe, but for example may without limitation include microwave ablation probes, laproscopic probes, other percutaneous probes or other internally inserted compression devices. The present invention is not limited to quasi-static compressions, but can be used with low frequency vibration compressions of a single frequency or chord of frequencies introduced through the probe 10 in which case Doppler readings of shear waves may be obtained from the ultrasound device. Low frequency vibration may also be used in the present invention to generate MRI elastograms by developing data over k-space. Generally, the tines 14 need not be extended from the probe 10 after the lesion has begun and may be optional if sufficient friction exists between the probe 10 and tissue. The elastogram may also be used to visualize the tumor before RF ablation.

[0078] It is specifically intended that the present invention not be limited to the embodiments and illustrations contained herein, but that modified forms of those embodiments including portions of the embodiments and combinations of elements of different embodiments also be included as come within the scope of the following claims.

CLAIMS

WE CLAIM:

1. A method of monitoring RF ablation of tissue comprising the steps of:

(a) inserting an ablation electrode into an ablation region of the tissue and applying an RF ablation current to the ablation region;

(b) obtaining a baseline image of the region indicating tissue location;

(c) applying compression to the region;

(d) obtaining a compression image of the region indicating new tissue locations; and

(e) processing the baseline and compression images to obtain an image indicating elasticity of the tissue in the region such as may demarcate the lesion formed by the RF ablation.

2. The method of claim 1 wherein step (c) is performed by movement of the ablation electrode.

3. The method of claim 1 wherein the ablation electrode is substantially inflexible in use to reduce shifting of the tissue perpendicularly to the compression.

4. The method of claim 1 wherein the RF ablation current is applied after steps (b)-(e).

5. The method of claim 1 wherein the RF ablation current is applied during and after the steps (b)-(c).

6. The method of claim 1 wherein the RF ablation current is applied before steps (b)-(c).

7. The method of claim 1 wherein the images are obtained using ultrasonic imaging techniques and including the steps repeating at least one of steps (b) and (d) at periodic intervals to obtain a measurement of temperature increases in the tissue caused by the RF ablation.

8. The method of claim 7 including at step (e) correcting at least one of the images by inferred speed of sound changes caused by changes in tissue temperature.

9. The method of claim 7 further including the step of displaying an image of temperatures.

10. The method of claim 1 including the step of monitoring periodic physiological motion and wherein steps (c) and (d) are timed to occur in periods of minimal periodic physiological motion.

11. The method of claim 1 including the step of monitoring periodic physiological motion and wherein step (c) is timed to occur in periods of low compression caused by the periodic physiological motion and (d) are timed to occur in periods of high compression caused by the periodic physiological motion.

12. The method of claim 1 including the steps of repeating steps (b) and (c) to obtain images of adjacent planes through the tissue to produce a three-dimensional image indicating elasticity of the tissue in the region.

13. The method of claim 12 wherein the adjacent planes are selected from the group consisting of: parallel planes obtained by translating an ultrasonic transducer and fan-arrayed planes obtained by tilting an ultrasonic transducer at small angles.

14. The method of claim wherein the ultrasonic transducer is selected from the group consisting of: 1D, 1.5D and 2D transducers.

15. A method of medical imaging comprising the steps of:

(a) inserting a probe into a region of tissue to be imaged;

(b) compressing tissue of the region using the probe;

(c) obtaining at least one image of the region indicating tissue movement under compression by the probe; and

(d) processing the image to obtain an indication of elasticity of the tissue in the region.

16. The method of claim 15 wherein the tissue is an *in vivo* organ.

17. The method of claim 15 wherein the probe is substantially inflexible in use to reduce shifting of the tissue perpendicularly to the compression.

18. The method of claim 15 wherein the probe is an electrode for radio frequency ablation and including the step of ablating tissue in the region before obtaining the image.

19. The method of claim 15 wherein the probe is an electrode for radio frequency ablation and including the step of ablating tissue in the region during the obtaining of the at least one image.

20. The method of claim 15 wherein the images are obtained using an image modality selected from the group consisting of: computed tomography imaging, magnetic resonance imaging, and ultrasonic imaging.

21. The method of claim 20 wherein the images are obtained using ultrasonic imaging techniques applying ultrasonic energy propagating along an insonification axis and wherein the probe compresses the tissue along the insonification axis.

22. The method of claim 21 wherein the probe is inserted along the insonification axis.

23. The method of claim 15 wherein step (c) further comprises:

obtaining a baseline image of the region prior to compression indicating tissue locations; and

obtaining a compression image of the region indicating tissue locations; and

wherein step (d) processes the baseline and compression images to obtain an image indicating elasticity of the tissue in the region.

24. The method of claim 23 wherein the determination of elasticity includes the step of computing the gradient in tissue movement, where tissue movement is

measured within the region by finding the maximum correlation in corresponding first and second portions of the baseline and compression images as a function of displacement of one portion with respect to the other.

25. The method of claim 23 wherein the determination of elasticity includes the step of determining the maximum correlation in the spectra of the baseline and compression images as a function of displacement of one spectrum with respect to the other.

26. The method of claim 15 wherein including obtaining a series of images in adjacent parallel planes through the tissue to produce a three-dimensional image indicating elasticity of the tissue in the region.

27. An apparatus for producing elastographic images of internal structures comprising:

a probe insertable into the body to a region of the internal body structure;

a compression fixture holding the probe to apply a controlled compression to the region during image acquisition of the region.

28. The apparatus of claim 27 wherein the probe includes means for gripping the body structure after insertion.

29. The apparatus of claim 27 wherein the compression fixture moves the probe along the axis of insertion by a predetermined amount.

30. The apparatus of claim 27 wherein the predetermined amount is substantially less than 2% of the length of the internal body structure being images.

31. The apparatus of claim 27 wherein the compression fixture includes an electronic actuator.

32. The apparatus of claim 27 further including a controller communicating with the compression fixture and an ultrasonic imaging system to obtain ultrasonic images before and after compression using the compression fixture.

33. A method of three-dimensional medical imaging of *in vivo* tissue comprising the steps of:

(a) obtaining a baseline image of the tissue along a plane through the tissue;

(b) compressing the tissue;

(c) obtaining a compression image of the tissue along the plane through the tissue;

(d) processing the baseline and compression images to obtain an image indicating elasticity of the tissue in the plane;

(e) repeating steps (a)-(d) for a set of adjacent planes; and

(f) displaying a three-dimensional representation of the *in vivo* tissue;

wherein the tissue is a lesion and including the step of calculating the lesion volume.

34. A method of monitoring RF ablation of tissue comprising the steps of:

(a) inserting an ablation electrode into an ablation region of the tissue;

(b) applying an RF ablation current to the ablation region;

(c) obtaining ultrasound images of the region at periodic intervals indicating apparent tissue locations; and

(e) processing the images to obtain displacement images.

(f) accumulating displacement from displacement images.

(g) taking the gradient of the accumulated displacements at specified times to obtain images indicating temperature of the tissue in the region such as may demarcate the lesion formed by the RF ablation.

35. A method of monitoring RF ablation of tissue comprising the steps of:

(a) inserting a percutaneous probe into a region of the tissue;

(b) introducing a low frequency vibration or oscillation of the probe using a single frequency or a chord of frequencies;

(c) imaging the mechanical shear waves generated using Doppler techniques; and

(d) processing the Doppler information to generate images indicating tissue stiffness or elasticity.

36. A method of monitoring RF ablation of tissue comprising the steps of: inserting a percutaneous probe into a region of the tissue:

(a) introducing a low frequency vibration or oscillation of the probe.

(b) fill k-space information during similar phases in the vibration for MR elastography; and

(c) process the k-space information to generate MR elastograms.

FIG. 1

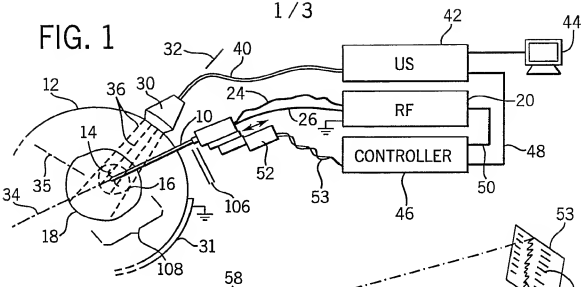


FIG. 2

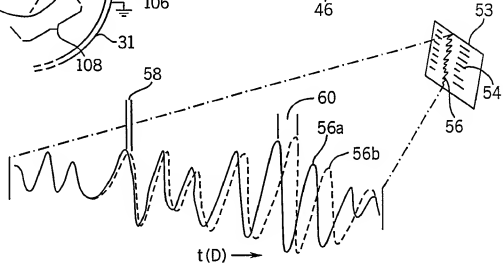


FIG. 3

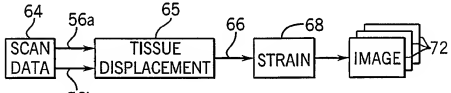
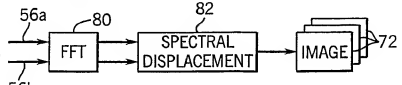


FIG. 4



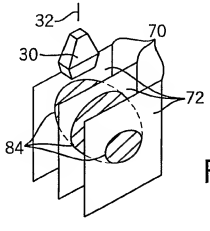


FIG. 5

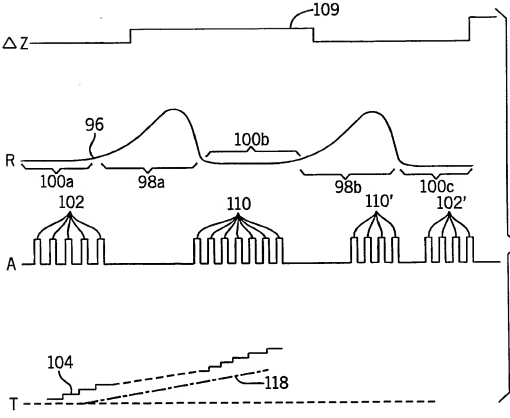


FIG. 6

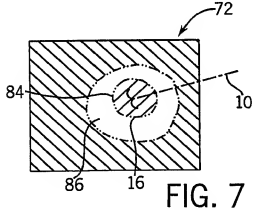


FIG. 7

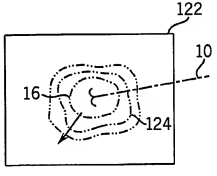


FIG. 8

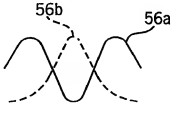


FIG. 9

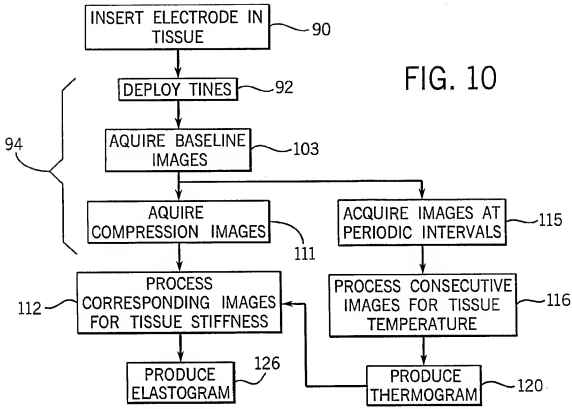

INSERT ELECTRODE IN TISSUE
90
DEPLOY TINES
92
94
AQUIRE BASELINE IMAGES
103
AQUIRE COMPRESSION IMAGES
111
ACQUIRE IMAGES AT PERIODIC INTERVALS
115
112
PROCESS CORRESPONDING IMAGES FOR TISSUE STIFFNESS
PROCESS CONSECUTIVE IMAGES FOR TISSUE TEMPERATURE
116
PRODUCE ELASTOGRAM
126
PRODUCE THERMOGRAM
120

FIG. 10

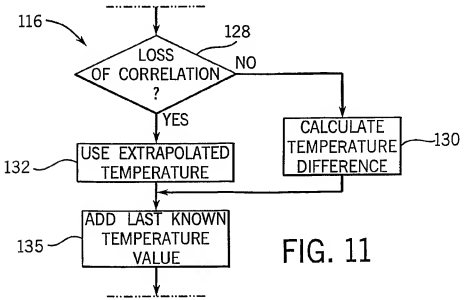

116
128
LOSS OF CORRELATION ?
NO
YES
CALCULATE TEMPERATURE DIFFERENCE
130
132
USE EXTRAPOLATED TEMPERATURE
ADD LAST KNOWN TEMPERATURE VALUE
135

FIG. 11

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 03/04413

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61B8/08 A61B8/14 G01S15/89

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61B G01S

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01 06927 A (ARTANN LAB) 1 February 2001 (2001-02-01)	27,29-31
A	page 6, line 8 -page 8, line 23 page 10, line 30 -page 14, line 10; figures 1,4A,6	32
X	US 5 265 612 A (SARVAZYAN ARMEN P ET AL) 30 November 1993 (1993-11-30) column 2, line 14 -column 5, line 12; figures 1,2	27,31,32
X	EP 0 920 833 A (WIEBE PETER ;LORENZ ANDREAS (DE); ERMERT HELMUT INST FUER HOCHFR () 9 June 1999 (1999-06-09)	27,31
A	column 2, line 46 -column 5, line 24; figures 1,2	32

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
4 June 2003	25/06/2003

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Artikis, T

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 03/04413

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 1-26, 33-36
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery

2. [ ] Claims Nos.:
because they relate to parts of the international Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

nation on patent family members

International Application No
PCT/US 03/04413

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0106927 A	01-02-2001	US 6142959 A	07-11-2000
		AU 6114600 A	13-02-2001
		JP 2003505134 T	12-02-2003
		WO 0106927 A1	01-02-2001
US 5265612 A	30-11-1993	WO 9414379 A1	07-07-1994
EP 0920833 A	09-06-1999	DE 19754085 A1	10-06-1999
		EP 0920833 A1	09-06-1999

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
27 December 2001 (27.12.2001)

PCT

(10) International Publication Number
WO 01/97702 A1

(51) International Patent Classification[7]: A61B 18/18

(21) International Application Number: PCT/US01/19454

(22) International Filing Date: 19 June 2001 (19.06.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
09/598,124 21 June 2000 (21.06.2000) US

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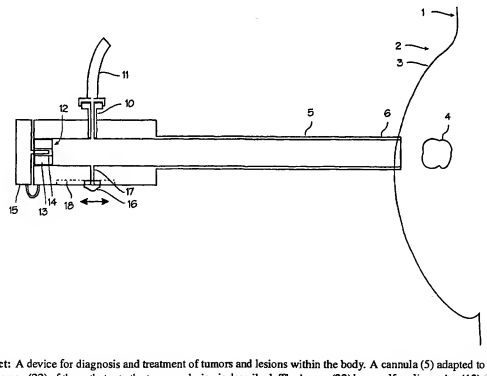
(74) Agent: CROCKETT, K., David; Crockett & Crockett, 24012 Calle de la Plata, Suite 400, Laguna Hills, CA 92653 (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

[Continued on next page]

(54) Title: DEVICE FOR BIOPSY AND TREATMENT OF BREAST TUMORS



(57) Abstract: A device for diagnosis and treatment of tumors and lesions within the body. A cannula (5) adapted to apply suction through the lumen (22) of the catheter to the tumor or lesion is described. The lumen (22) has a self sealing valve (12) through which a cryoprobe (27) is inserted while the suction is being applied. The cryoprobe (27) is then inserted into the lesion, and operated to ablate the lesion.

WO 01/97702 A1

Published:

— *with international search report*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

Device for Biopsy and Treatment of Breast Tumors

Field of the Inventions

The devices and method described below relate to the diagnosis and treatment of breast lesions, and more generally, to the diagnosis and treatment of tumors and lesions throughout the body.

Background of the Inventions

Biopsy is an important procedure used for the diagnosis of patients with cancerous tumors, pre-malignant conditions, and other diseases and disorders. Typically, in the case of cancer, when the physician establishes by means of procedures such as palpation, mammography or x-ray, or ultrasound imaging that suspicious circumstances exist, a biopsy is performed. The biopsy will help determine whether the cells are cancerous, the type of cancer, and what treatment should be used to treat the cancer. Biopsy may be done by an open or percutaneous technique. Open biopsy, which is an invasive surgical procedure using a scalpel and involving direct vision of the target area, removes the entire mass (excisional biopsy) or a part of the mass (incisional biopsy). Percutaneous biopsy, on the other hand, is usually done with a needle-like instrument through a relatively small incision, blindly or with the aid of an imaging device, and may be either a fine needle aspiration (FNA) or a core biopsy. In FNA biopsy, individual cells or clusters of cells are obtained for cytologic examination and may be prepared such as in a Papanicolaou smear. In core biopsy, as the term suggests, a core or fragment of tissue is obtained for histologic examination which may be done via a frozen section or paraffin

section. One important area where biopsies are performed is the diagnosis of breast tumors.

Traditionally, the biopsy technique for breast tumors involves placing a biopsy device multiple times into the breast and taking several samples of tissue from a mass or tumor which is suspected of being cancerous. Several samples are required to be sure that some tissue from the suspect mass has been captured, and enough tissue has been sampled to ensure that, if disperse cancer cells exist in the suspect mass some of those cancer cells will be captured in the samples. Each time the device is placed the physician must locate and direct the device with ultrasound imaging into the correct position near the suspect mass. Some breast tumors and lesions are very well defined, hard spherical masses which grow within the soft, compliant breast tissue. It is difficult to force a needle into these lesions because they are resistant to puncture and fairly mobile. Forcing the biopsy needle into the lesion is like trying to spear an apple floating in water.

Vacuum assisted biopsy system proposed by Biopsys involves sucking a breast lesion into a cannula and shearing off the captured edge of the lesion to obtain a biopsy sample. The device uses a vacuum to collect tissue into the side of an open tubular device, and then uses a rotating corer to cut the tissue collected. The rotating core is slidable within the tubular section and can be pulled back to remove the tissue collected in the rotating core. An additional stylet inside the rotating core can be used to push the tissue out of the core. The device can be rotated on its axis to remove a sample, 360 degrees around the central placement of the device. Typically, physicians sample six to eight cores. One advantage of this device is that the physician does not have to remove the device for additional biopsy samples. However,

the tumor itself must be re-engaged after every coring operation, which entails substantial effort in relocation and confirmation that the target suspect mass has been engaged by the side aperture. Tumors may be too tough to yield to the suction and deform as necessary to enter the side opening of the cannula. Doctors also currently use the device to take a circular sequence of cores by rotating the device about its long axis or by sideways movement of the suction head to take a line of cores.

After biopsy and analysis, the tumor must be treated with a separate device, as Biopsys teaches that their coring device should not be used for resection. Indeed, the device is not designed to perform resection with assurance that complete resection of a suspect mass has been accomplished. Mechanical cutting and disruption of the tissue structure and cancer cell dispersion (that is, tearing of the tissue around the cancer and movement of the cancer cells amongst normal tissue) will result in unintentional delivery of cancer cells into healthy tissue adjacent the lesion.

Summary

The devices and methods described below provide for diagnosis and treatment of tumors within the breast. The devices include structures which permit the surgeon to secure a suspect mass or tumor within the breast for an extended period of time and for several biopsies, coring procedures, or resections. The suspect mass or tumor is secured to a cannula for the entire diagnostic and treatment procedure, or subsets of the procedure such as biopsy or ablation. This allows the placement of the cannula with a single step utilizing methods such as ultrasound to guide the cannula toward the tumor.

The cannula includes a lumen adapted to be connected to a source of vacuum, which can be used to secure a breast lesion

to the cannula. A ring seal on the proximal end of the catheter permits biopsy needles, cryoprobes or other ablation devices to be inserted through the cannula and into the lesion while the vacuum on the cannula is maintained. In this manner, the needles and ablation devices may be inserted into the lesion while the lesion in held securely in place by the suction applied to the cannula.

Brief Description of The Drawings

Figure 1 illustrates the cannula adapted for use in securing a breast tumor during a biopsy or ablation procedure.

Figure 2 illustrates the biopsy needle in use with the cannula of Figure 1.

Figure 3 illustrates a multiple coring needle which may be used with the cannula of Figure 1.

Figure 4 illustrates the placement of a cryoprobe or other ablative device within the cannula of Figure 1.

Figure 5 illustrates a method of breast tumor ablation for tumors located near the skin.

Figure 6 illustrates a method of breast tumor ablation for tumors located near the skin.

Figure 7 illustrates and adaptation of the cannula to provide additional protection to the skin.

Detailed Description of the Inventions

Figure 1 illustrates the biopsy and treatment device adapted for use in securing a breast tumor during the biopsy and treatment procedure. The patient **1** and the patient's breast **2** and skin **3** of the breast are shown schematically. The tumor, lesion or other suspect mass **4** is located within

the breast, surrounded by soft tissue and fatty tissue. The tumor in this illustration is a well defined, hard mass ranging in size from 3 to 40 mm in diameter, typical of a benign palpable tumor or fibro-adenoma, although the device and method may be used to treat fibrocystic disease and other conditions. The device comprises a cannula **5** with a straight cut distal edge **6** adapted for insertion through a small incision in the skin overlying the tumor and a proximal end **7** which remains outside the breast. The proximal end of the cannula is fitted with hub **8** which serves as a handle and a manifold for the several connections to the cannula. This hub may be integral with the cannula or provided as a separate piece secured to the proximal end of the cannula. The cannula has a lumen **9** extending through the cannula from the distal edge to the proximal end of the cannula. On the hub, a vacuum connection **10** in the form of Luer fitting provides a fluid connection between the lumen of the cannula and a vacuum tube **11**. The vacuum hose may be connected to any source of vacuum or suction. On the proximal end of the hub, a valve **12** seals the cannula proximal end against air pressure but allows passage of the needles and probes used in the procedure. The valve may be a self-sealing silicone plug **13** provided with a slit **14** capable of accommodating the needles and probes by resiliently expanding and conforming around a needle or probe when a needle or probe is forced through the slit, and resiliently closing to an airtight seal when the needles or probes are removed. Thus, the valve allows for insertion of various instruments and elongate medical devices while maintaining the seal necessary to provide sufficient suction to hold the tumor. A stopper or cap **15** is provided for insertion into the slit when the valve is not occupied by a needle or probe to positively seal the valve. A backup valve, such as ball valve which opens to form a clear and straight lumen, may be placed in line before the valve 12 in place of

the stopper. The cannula is made of an acceptable biological material such as Teflon, carbon fiber, metal or metal composite for maximum strength with minimal wall thickness. The self-sealing valve is comprised of silicone or other material of similar resilience and conformability. An additional valve **16** may be added on the proximal handle, controlling a port **17** communicating between the vacuum lumen and the exterior of the cannula. The valve illustrated is merely a thumbslide mounted in a recess **18**. This valve may be used to break the vacuum established in the vacuum lumen to release a lesion from the distal tip of the device, or to bleed the vacuum from the lumen to lessen the suction on a lesion.

Figure 2 illustrates the cannula in use with a biopsy needle **20** in place within the lumen. A biopsy needle 20 fits within the lumen of the cannula and passes through the valve 12. The valve deforms and opens enough to allow the needle to pass through, yet still maintains a sufficiently airtight seal to maintain the vacuum within the cannula lumen. The needle has a sharp distal tip **21** which can pierce the tumor 4. The distal tip is shaped with a coring edge to collect tissue within the lumen **22** of the needle. As depicted in Figure 2, suction has been applied to the cannula lumen through the vacuum hose 11 and connection 10, thus drawing the tumor to the distal edge of the cannula and securely holding it in place. The biopsy needle has been inserted through the self-sealing valve and through the cannula lumen into and through the tumor. A small core of tumor tissue **23** has been forced into the lumen of the needle. The needle may now be removed and the core of tumor tissue extracted and analyzed for the presence of cancer cells. When the needle is removed, the suction is maintained on the cannula lumen and the tumor remains securely engaged with the cannula distal edge. The biopsy needle (or another) can then be inserted through the

cannula and into the tumor without having to relocate and reengage the tumor with the cannula. After all necessary biopsies have been taken, the sample tissue may be analyzed for the presence of cancer cells or other undesirable tissue for which ablation is indicated.

Figure 3 illustrates a multiple coring needle **24** for use with the system. This needle includes several coring lumens **25** opening at the distal end of the needle into coring edges **26**. The coring lumens are spaced in a circle about the circumference of the needle, and extend from the distal tip 21 of the needle proximally to the proximal end of the needle. It may be used in place of the single biopsy coring needle as illustrated in Figure 2. By providing suction to one or more of the lumens, the tumor is secured to the coring needle.

Figure 4 illustrates the use of an ablative device, such as cryoprobe, with the cannula. The cryoprobe **27** fits within the lumen of the cannula and passes through the valve 12, and the distal tip of the cryoprobe is forced into the tumor until the active freezing portion of the probe resides within the tumor. During placement of the cryoprobe, the vacuum is maintained within the lumen so that the tumor is securely engaged by the cannula. With the tumor secured by the vacuum, the cryoprobe may be easily forced into the tumor. The cryoprobe may be operated to ablate the tumor with cryogenic freezing as required to destroy the tumor. To operate the cryoprobe, liquid or gas cryogenic fluids (such as liquid nitrogen, or gaseous argon in combination with a Joule-Thomson cryostat in the probe tip) are passed through the probe, supplied from a cryosurgical control system (not shown). The operation of the cryoprobe creates an iceball **28** which encompasses the lesion 4, and cools the lesion to lethal cryogenic temperatures. Any ablation device may be used in place of the cryoprobe, including RF ablation probes,

microwave ablation probes, laser ablation probes, or focused ultrasound energy probes. Temperature sensors **29** may be mounted on the skin over the lesion in order to monitor skin temperature, so that the surgeon may avoid ablating the skin.

In use, the devices described above are used in place of traditional biopsy, coring and ablation devices. Prior to use, the patient is prepared and the breast is appropriately prepped and draped. The site is prepared using local anesthesia and, optionally, intravenous sedation. The patient is positioned on an operating table in the supine position, with the patient on her back. (If the procedure is accomplished under stereotactic guidance, the patient may be prone on a stereotactic table, exposing the breast below the table.) The breast is imaged, if not previously imaged, to determine the location of lesions. A small incision is made in the breast to allow the cannula to be easily inserted into the skin. The surgeon inserts the cannula into the patient's breast through the incision, pushes it into the breast until the distal edge of the cannula is proximate to the boundary of the tumor. An ultrasound scanner, MRI, stereotactic, mammographic, infrared or other imaging device is used to obtain an image of the breast, including the tumor and any device inserted into the breast, and the surgeon uses the display from the imaging device to assist in guidance of the cannula to the tumor. With the cannula distal edge in position near the tumor, the surgeon applies vacuum to the cannula through the side port on the cannula. The vacuum draws the tumor toward the cannula, and the cannula securely engages the tumor until the suction is broken at the end of the procedure. The surgical biopsy needle can be inserted through the cannula and into the tumor to retrieve a sample of tissue for analysis. Because coring can be accomplished without removing the portion of the tumor engaged by the cannula, or otherwise disrupting the suction between the

cannula and the tumor, several biopsy samples may be taken without having to relocate and re-engage the tumor.

Depending on the analysis of the biopsy (whether or not the samples obtained contain cancerous cells or other conditions), treatment of the tumor may be required. If analysis can be accomplished intra-operatively (that is, during a period of time in which it is feasible to keep the patient in the operating room and maintain the tumor engaged with the cannula), and indicates the presence of cancerous cells or other condition for which ablation is indicated, an ablation instrument can be inserted through the cannula and into the tumor. If so, the surgeon inserts an ablation instrument, such as a small caliber cryoprobe, into the tumor. Preferably, the surgeon inserts a cryoprobe through the valve and cannula and into the tumor, while maintaining suction on the cannula. The surgeon initiates cooling of the cryoprobe, and cools the tumor through one or more cycles of cooling to cryogenic temperatures and subsequent warming and thawing. A double freeze-thaw cycle is currently recommended. Each cycle consists of a 6 to 15 minute freeze followed by thawing until the internal cryoprobe temperature reaches 0°C (approximately 6 to 15 minutes). The device may also be used without regard to biopsy results. Patients prefer to have these lesions treated, even if they prove to be benign. In current practice, should biopsy results indicate the presence of cancer, the patient must return to the operating room shortly after the biopsy, undergo preparation, anesthesia, relocation of the lesion and ablation. Instead, the lesions may be ablated intraoperatively with the biopsy, immediately after biopsy and without interrupting the procedure to await the biopsy results. Should the biopsy prove negative for the presence of cancer, the patient will have received a substantially cosmetic treatment. Should the biopsy prove positive, the patient will have received a necessary

therapeutic procedure. In addition to the ablative procedure, the positive biopsy may indicate the need for additional monitoring and treatment.

For lesions deeper than 1 cm from the skin surface, the cryoprobe is advanced until the distal tip is located approximately in the center of the lesion or just beyond the lesion. For smaller lesions (<2cm diameter) the ice ball may grow beyond the margins of the tumor, while for larger lesions, the ice ball may remain within the confines of the tumor. The cryoprobe tip temperatures and skin mounted thermocouple readings are monitored throughout the ablation procedure. If the temperature of the skin overlying the cryoprobe measures below freezing, freezing operation of the cryoprobes should be paused until it returns to 10°C (the temperature at the edge of the ice ball edge is 0°C and exposure to such a temperature for the few minutes will not harm the skin, but caution should always be employed).

The procedure may be augmented with additional steps. Just prior to ablation treatment, prophylactic antibiotics can be administered at the surgeon's discretion. Just prior to cryosurgical ablation, cryogenic enhancement agents may be injected directed into the tumor through a hypodermic needle inserted through the valve and cannula and into the tumor while it is secured by suction to the cannula. During cooling operation of the cryoprobes, warm saline may be washed over the skin overlying the tumor and iceball to prevent freezing of the skin.

If the lesion being treated is close to the skin such that cryoablation of the lesion entails a danger of cryoablation of the overlying skin, several milliliters of a resorbable material such as sterile saline may be injected or inserted into the subcutaneous tissue between the skin and the

lesion. This will create a thermally protective mass or barrier layer between the tumor and the skin. Thermal protection may arise from insulative effect of the thermally protective mass or merely by the distension or separation of the skin away from the tumor and thus away from the iceball. As illustrated in Figure 5, where the tumor 4 is close to the skin 3, the thermally protective mass **30** is injected between the skin 3 and the subcutaneous fat **31** of the breast. When the cryoprobe 27 is operated to create the iceball, the iceball **32** either grows into the thermally protective mass or is inhibited in growth in the direction of the thermally protective mass (as illustrated by the non-spherical shape of the iceball in this illustration). This method basically distends the skin away from the iceball. This may also be accomplished by dissecting the skin away from the tumor with a balloon inserted between the skin and fat in the area overlying the tumor. Balloon dissection can be accomplished as illustrated in Figure 6. Here, a balloon **33** has been inserted subcutaneously between the tumor **4** and the overlying skin **3**. The balloon is inflated with air or other sterile gas, through inflation tube **34**, creating a good layer of insulation between the cryoprobe and the overlying skin.

Figure 7 illustrates and adaptation of the cannula to provide additional protection to the skin. The cryoprobe 27 is inserted through a side lumen **35** provided on the cannula 5. The breast lesion 4 is drawn by vacuum to the tip of the cannula. The cryoprobe is advances distally out of the side lumen until the freezing region underlies the lesion, and it operated to create the iceball **36**. The iceball extends superficially toward the skin and to encompass the lesion, and also extends posteriorly into the breast, where some healthy breast tissue is ablated but the overlying skin is not. This system and procedure also has the advantage that the lesion itself is not punctured, limiting the potential for seeding

due to the release of cancerous cells from the disruption of the tissue of the tumor.

The cannula illustrated above is preferably 10 to 20 cm in length and about 3 mm in diameter with an internal diameter of 2.8 mm, and a clearance of about .25 mm between the inner bore of the cannula and any device inserted through the cannula during suction. The cryoprobes may be Joule-Thomson probes, liquid cryogen probes, or probes of other designs. Various other ablative devices may be used in place of the cryoprobe, including laser ablation devices, RF ablation devices, chemical ablation catheters and any other ablative technology proposed for use to destroy tumors and lesions. The vacuum applied is preferably in the range of 14 to 21 inches of mercury vacuum.

The devices and methods illustrated above have been illustrated in relation to the treatment of tumors and lesions within the breast. However, they may be used to treat tumors and lesions throughout the body wherever the tumors which are difficult to secure and locate are encountered, and wherever nearby tissue must be protected from freezing. Thus the devices and methods may be used for tumors and lesions of the uterine tube (such as uterine fibroids), kidney, liver, prostate or brain.

Thus, while the preferred embodiments of the devices and methods have been described in reference to the environment in which they were developed, they are merely illustrative of the principles of the inventions. Other embodiments and configurations may be devised without departing from the spirit of the inventions and the scope of the appended claims.

We claim:

1. A device for performing a biopsy of a mass within the breast of a human patient, said device comprising:

a cannula adapted for insertion into the body of the patient, said cannula having a distal end and a proximal end, and a lumen extending through the cannula and defining a proximal opening and a distal opening in the cannula;

a fitting disposed on the proximal end of the cannula, said fitting adapted for connection to a vacuum source;

an airtight seal in the proximal opening of the cannula, said airtight seal permitting passage of needles and cryoprobes through the seal while substantially maintaining the airtight seal.

2. A system for treating or sampling of a mass within the breast of a human patient, said system comprising:

a cannula adapted for insertion into the body of the patient, said cannula having a distal end and a proximal end, and a lumen extending through the cannula and defining a proximal opening and a distal opening in the cannula;

a fitting disposed on the proximal end of the cannula, said fitting adapted for connection to a vacuum source;

an airtight seal in the proximal opening of the cannula, said airtight seal permitting passage of elongate medical devices through the seal while substantially maintaining the airtight seal;

a source of vacuum pressure operably connected to the fitting;

an elongate medical device capable of insertion through the airtight seal and into the cannula, said elongate medical device being long enough to extend from the proximal end of the cannula to a distance outside the distal opening of the cannula.

3. The system of claim 2 wherein the elongate medical device is a biopsy needle.

4. The system of claim 2 wherein the elongate medical device is a cryoprobe.

5. The system of claim 2 wherein the elongate medical device is an ablation device suitable for ablation of the mass.

6. A method of performing cryosurgery of a lesion in the body of a patient, said method comprising;

inserting a cannula into the body of the patient so that the distal edge of the cannula is proximate the lesion;

applying suction to a lumen of the cannula, thereby drawing the lesion toward the cannula;

inserting an ablative medical device through the lumen of the cannula and into the lesion;

operating the ablative medical device to ablate the lesion.

7. A method of performing cryosurgery of a lesion in the body of a patient, said method comprising;

inserting a cannula into the body of the patient so that the distal edge of the cannula is proximate the lesion;

applying suction to a lumen of the cannula, thereby drawing the lesion toward the cannula;

inserting a cryoprobe through the lumen of the cannula and into the vicinity of the lesion;

operating the cryoprobe to ablate the lesion.

8. A method of performing cryosurgery of a lesion in the breast of a patient, the lesion being located under a portion of overlying skin, said method comprising;

providing a cannula, said cannula having a distal tip and a lumen adapted for application suction to the distal tip thereof, and inserting the cannula into the body of the patient so that the distal tip of the cannula is proximate the lesion;

applying suction to a lumen of the cannula, thereby drawing the lesion toward the distal tip cannula;

inserting a cryoprobe into the breast and into the vicinity of the lesion;

operating the cryoprobe to ablate the lesion.

9. The method of claim 8 further comprising:

inserting the cryoprobe into the lesion by inserting it through the lumen of the cannula and then advancing the cryoprobe distally from the lumen of the cannula and into the lesion.

10. The method of claim 8 further comprising:

inserting the cryoprobe into the lesion.

11. The method of claim 8 further comprising:

inserting the cryoprobe into the breast in a position posterior to the lesion.

12. The method of claim 8 further comprising:

placing a thermally protective mass between the lesion and the overlying skin prior to operating the cryoprobe to ablate the lesion.

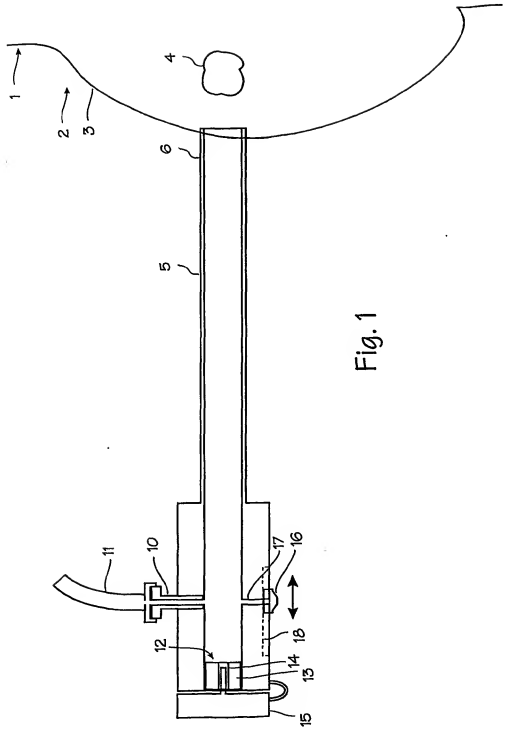


Fig. 1

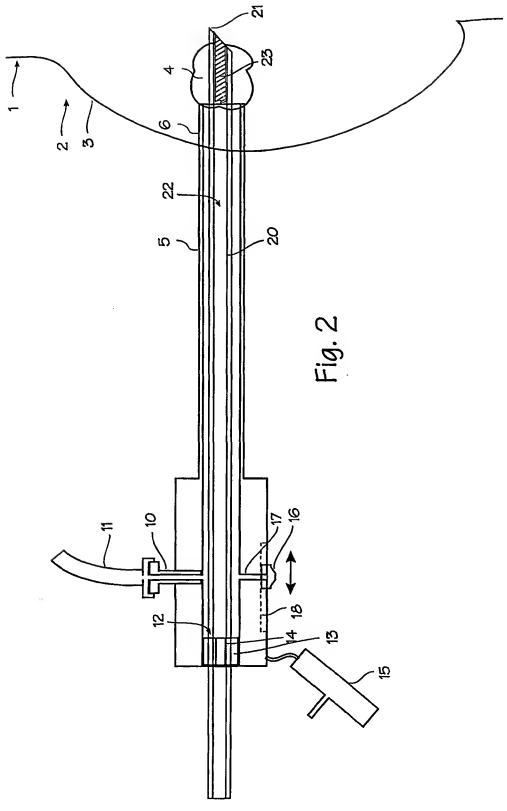


Fig. 2

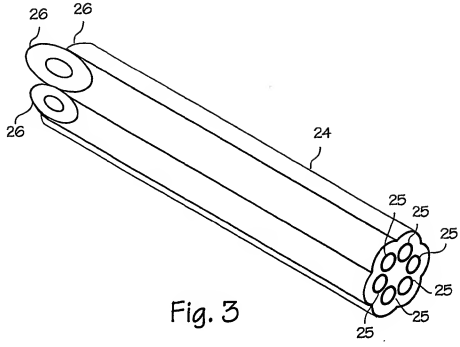


Fig. 3

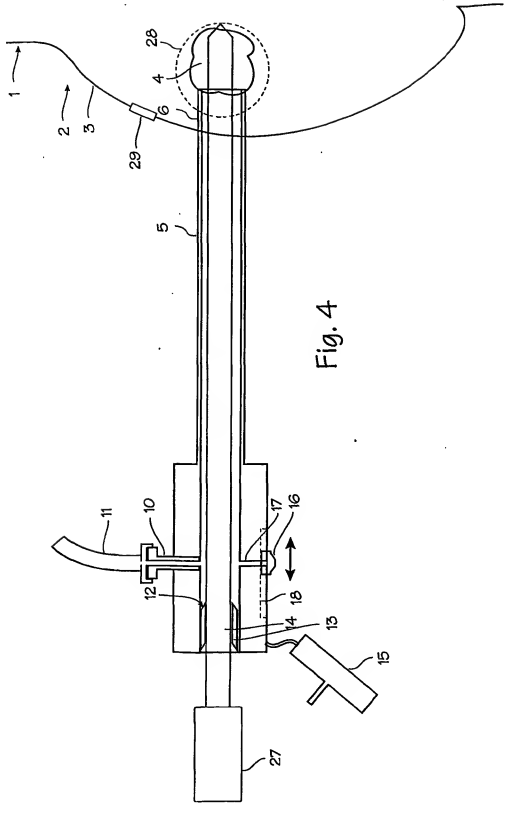


Fig. 4

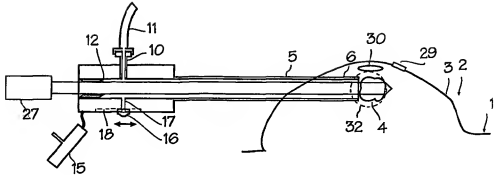


Fig. 5

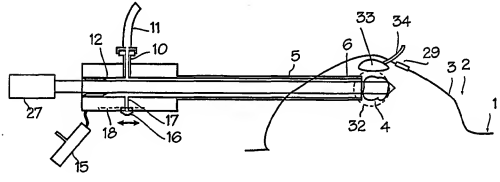


Fig. 6

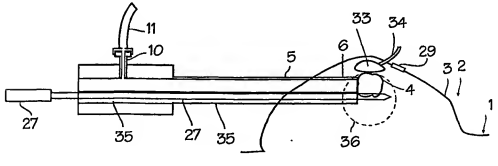


Fig. 7

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/19454

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :A61B 18/18
US CL :606/20

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 606/1, 20-26; 600/565-567

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,713,368 A (Leigh) 03 February 1998, whole document.	1-3
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Y		4-7
Y	US 6,032,675 A (Rubinsky) 07 March 2000, whole document, figure 2.	4-7

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

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"A"	document defining the general state of the art which is not considered to be of particular relevance		
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"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed	"&"	document member of the same patent family

Date of the actual completion of the international search 05 SEPTEMBER 2001	Date of mailing of the international search report 06 NOV 2001
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer MICHAEL PEFFLEY Diane Smith for Telephone No. (703) 308-0858

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